

**Amendments to the Specification:**

Please change paragraph [0000] to read as follows:

**[0000]** This application is the national stage filing under 35 U.S.C 371 of PCT/US 04/19812, which was filed on June 21, 2004, and which claims priority to U.S. provisional application 60/480,206, filed June 20, 2003.

Please change paragraph [0001] to read as follows:

**[0001]** Sexually transmitted diseases (STDs) are one of our major public health challenges. According to the Center for Disease Control, some STDs, such as syphilis and gonorrhea, have been brought to all time lows. However, strains of HIV resistant to currently used combination therapies are increasingly being identified, and there is a silent and growing epidemic of other STDs that pose equally difficult treatment and prevention challenges. These include genital herpes (HSV-2), Chlamydia and Papilloma. In the United States alone there are over 65 million people with an incurable STD <sup>[[1]]</sup>. STDs cause serious, life-threatening complications including cancers, infertility, ectopic pregnancy, spontaneous abortions, stillbirth, low birth weight, neurologic damage and death. Whether for a potentially curable or incurable disease a prophylactic approach for the prevention of the spread of STDs would save much human suffering and expense. Papilloma virus (PV), including human papilloma virus (HPV) have both human and veterinary significance, i.e., in cattle, horses, dogs, sheep and birds papilloma viruses in humans can cause dermal warts, and malignancies, including cervical cancer.

## **SUMMARY OF THE INVENTION**

Please change paragraph [0009] to read as follows:

**[0009]** CTC-96™ is one of a new family of chemical entities that are cobalt-containing Schiff base chelates, initially developed as anti-inflammatory agents, capable of scavenging superoxide radicals (US Patent 5,049,557), and subsequently found to have antiviral activity. These agents which do not react with nucleic acid bases are unlike nucleoside analog-type drugs in their mechanism of action. Neither do they act directly as protease inhibitors. Instead, they form stable adducts with the imidazole nitrogen of selected histidines in proteins <sup>[[2]]</sup>. They affect viral penetration and cell-to-cell spreading <sup>[[3]]</sup>. In addition, the drug acts intracellularly by inhibiting viral DNA replication albeit not via direct interaction with the nucleic acid. Because of their different mode of action, These compounds have also shown good efficacy against HSV-1 and HIV viral mutants that are resistant to currently used drugs.

Please change paragraph [00022] to read as follows:

**[00022]** CTC-96™ in saline was incubated with HPV-11 prior to infection of human neonatal foreskin fragments. The fragments were then grafted onto SCID mice. The animals were monitored weekly. They were weighed at the time of grafting, and every other week during the 12 weeks of the experiment. There was no effect of HPV-11 treatment by CTC96™ on the weight of the mice. The animals were sacrificed by cervical dislocation 12 weeks after graft implantation.

Length, width, and height of the graft were measured and recorded. A composite geometric mean diameter (cGMD) of the grafts was calculated for each mouse. The grafts were then removed and analyzed by histology, immunocytochemistry and RTPCR. Graft evaluation by immunocytochemistry utilized anti-common Papillomavirus antigen <sup>[[4]]</sup>. Explanted grafts were homogenized and total RNA was extracted. HPV-11 viral cDNA was generated by nested RT-PCR.

#### **Effect of CTC-96™ on Graft Size**

Please change paragraph [00033] to read as follows:

**[00033]** CTC-96™ has been found to be virucidal against Human Papilloma Virus(HPV) Type 11 <sup>[[5]]</sup> with no detectable effect on the growth of HPV-11-induced papillomas <sup>[[6]]</sup>. CTC-96™ neither decreased nor increased the growth of HPV-11-infected human papillomas. Given the virucidal activity of CTC-96™ a series of experiments was performed to evaluate the prophylactic activity of the compound under conditions resembling that of the use of a topical microbicide. When using a topical microbicide the target organ is first exposed to the microbicide before exposure to the virus. Various concentrations of CTC-96™ were evaluated in a model of HPV-11-infected human xenograft in the SCID mouse. The human grafts were exposed to CTC-96™ for 1 hour prior to exposure to HPV- 11 and engraftment. Because CTC-96™ is virucidal, it was washed off the foreskin fragments before exposure to the virus. The HPV-11-infected grafts were allowed to grow for 12 weeks. After 12 weeks, the animals were sacrificed and

the grafts recovered, measured and processed. Graft size, expressed as the composite geometric mean diameter of the two grafts borne by the animal, was the primary endpoint. Histology of the grafts was examined for the presence of HPV. Grafts were also processed for detection of HPV-11 mRNAs transcripts by reverse transcriptase-polymerase chain reaction (RT-PCR).

Please change paragraph [00040] to read as follows:

**[00040]** Bovine Papillomavirus Type 1 (BPV-1) was mixed with CTC-96™, incubated for 10 minutes at 37°C and then added to the cells. It is clear that CTC-96™ can inhibit the appearance of bovine Papillomavirus type 1 (BPV-1) induced transformation of C127 mouse epithelial cells in culture (Table 9).

**Table 9: CTC-96™ Inhibition of Bovine Papillomavirus Type 1 (BPV-1) Transformation of C127 Mouse Epithelial Cells in Culture: Exposure of Virus to Drug Prior to Infection. (Two experiments)**

Treatment	CTC- 96™ (mg/ml)	Number of Transformed Foci at 3 weeks	
		Exp. 1	Exp. 2
PBS alone	-	0	0
BPV-1 alone		96	105
CTC-96TH	0.1	68	80
CTC-96T <sup>m1</sup>	0.2	80	82
CTC-96TH	0.5	25	40